## REMARKS

Attached hereto is a marked-up version of the changes made to the Specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made." Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

### Comments Regarding Restriction Requirement

Applicants affirm the election, with traverse, of claims 8, 45-46, 48 and 50-57, corresponding to the invention of Group III. Applicants submit that claims 44, 47, 49, 58 and 59, drawn to methods of use of the antibodies of Group III, should be examined together, per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of product claims, for rejoinder of process claims covering the same scope of products. Moreover, Applicants reaffirm that the Patent Office position of subjecting the subject matter of SEQ ID NO:1 and SEQ ID NO:3 to a "restriction requirement" is improper. Rather, Markush practice for consideration of patentably distinct species should be followed. In this regard, see the response of March 7, 2002.

### Claim Objections

The Office Action states that claim 8 is objected to because it depends on non-elected claim 1. Claim 8 has been rewritten in independent form, thus obviating the objection.

The Office Action further notes that claim 48 is objected to under 37 CFR 1.75(c) as being of improper dependent form for allegedly failing to further limit the subject matter of a previous claim. In particular, the Office Action alleges that the recited limitation of claim 48, "wherein the antibody is labeled" fails to further limit the composition comprising the antibody in claim 46 which recites "[a] composition comprising an antibody of claim 8 and an acceptable excipient." This objection is respectfully traversed.

The antibody of claim 8, as amended, is set forth as:

"An isolated antibody selected from the group consisting of::

a) an antibody which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, wherein the antibody binds to an epitope of a polypeptide of SEQ ID NO:1 or SEQ ID NO:3, and

b) an antibody which specifically binds to a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, wherein the antibody binds to an epitope of a polypeptide having a naturally occurring amino acid sequence at least 90% identical to SEQ ID NO:1 or SEQ ID NO:3, said naturally occurring amino acid sequence having HS3C activity."

Claim 46 recites "[a] composition comprising an antibody of claim 8 and an acceptable excipient." Claim 48 is dependent upon claim 46 and further limits the composition as comprising an antibody that is labeled. Such labeling of antibodies is described in the Specification, for example, at p. 38, line 31 through p. 39, line 4:

> Diagnostic assays for HS3C include methods which utilize the antibody and a label to detect HS3C in human body fluids or extracts of cells or tissues. The antibodies may be used with or without modification, and may be labeled by joining them, either covalently or non-covalently, with a reporter molecule. A wide variety of reporter molecules which are known in the art may be used, several of which are described above.

The composition of claim 48 is thus distinguished from the composition of claim 46 by the further limitation that the antibody recited therein is modified by the addition of a label. It is therefore believed that this claim is in compliance with 37 CFR 1.75(c) and withdrawal of the objection is respectfully requested.

**Comments Regarding Information Disclosure Statement, PTO form 1449**

The Office Action states that "[t]he references cited on PTO 1449 filed 8/8/01 have been crossed out because none of the cited references have been submitted to the Office." (Office Action at p. 3, item 8.) Applicants respectfully submit that ***all*** of the references cited on PTO 1449 filed 8/8/01 were either previously submitted by Applicants in the priority applications or were cited to Applicants by the Examiner during the prosecution of the priority applications.

That is, items 1-8 on PTO 1449 filed 8/8/01 were previously submitted on 1/16/98 and were initialed by Examiner Kawai Lau on 6/25/98; items 9-10 on PTO 1449 filed 8/8/01 were cited to Applicants by Examiner Kawai Lau on PTO-892 sent with an Office Action dated 7/2/98; item 11 on PTO 1449 filed 8/8/01 was cited to Applicants by Examiner Kawai Lau on PTO-892 sent with an Office Action dated 1/6/99. (Copies of all forms PTO 1449 and PTO-892 referenced above are attached.)

Initially, it is noted that the Examiner failed to completely examine Applicants' invention. Specifically, Applicants object to the Examiner's failure to obtain and fully consider the references cited in the parent application and listed on the Form 1449. According to M.P.E.P. § 609:

> ...the examiner ***will consider*** information which has been considered by the Office in a parent application when examining (A) a continuation application filed under 37 CFR 1.53(b) or filed under former 37 CFR 1.60, (B) a divisional application filed under 37 CFR 1.53(b) or filed under former 37 CFR 1.60, or (C) a continuation-in-part application (see MPEP Section 201.06(b)) filed under 37 CFR 1.53(b), and a list of the information need not be submitted in the continuation, divisional, or continuation-in-part application unless applicant desires the information to be printed on the patent. (Emphasis added)

As can be seen from the above, it is mandatory for the Examiner to consider information previously considered in a parent application. The Patent Office has facilities for obtaining copies of the cited information and it is urged that the Examiner make use of these facilities. It is not reasonable, or required by Patent Office policy, for Applicants to provide additional copies of documents already considered in a parent application, especially in view of the vast number of pending applications that Applicants' Assignee, *Incyte Genomics, Inc.*, has at the Patent Office. Refusal by the Examiner to obtain and consider the documents cited in the parent application clearly is not consistent with Patent Office procedures.

**Enablement Rejection under 35 U.S.C. § 112, first paragraph**

Claims 8, 45-46, 48 and 50-57 stand rejected under 35 U.S.C. 112, first paragraph allegedly for lacking an enabling disclosure with respect to variants and biologically active and immunogenic fragments of SEQ ID NO:1. The Examiner has specifically stated that "[t]he specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with the claims." (June 3, 2002 Office Action, at page 4). The Examiner further states "[t]he specification does not teach how to make and use *any* antibody that binds to a polypeptide comprising a) *any* naturally-occurring amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 1 and 3, b) *any* biologically active fragment of the polypeptide "having" an amino acid sequence of SEQ ID NO:1 and 3, c) *any* immunogenic fragment of the polypeptide "having" an amino acid sequence of SEQ ID NO: 1 and 3 since neither the structure nor function of any amino acid sequence mentioned above is provided." (June 3, 2002 Office Action, at page 5). Applicants respectfully traverse this rejection.

The Specification provides extensive teaching on how to make and use antibodies, see for example page 9, lines 1-9, page 31, lines 20-25, and page 38, line 27 to page 39, line 4. Further, the Specification describes how to make variants to the amino acid sequence of SEQ ID NO:1, including variants having 90% sequence identity to SEQ ID NO:1, as well as to fragments of SEQ ID NO:1 having biological or immunogenic activity (see page 3, lines 12-20, page 8, lines 16-22 and page 14, line 23 to page 15, line 1). Thus on this basis, one skilled in the art would know how to make and use antibodies to variants and fragments of SEQ ID NO:1. This is further evidenced by the fact that the specification describes the production of antibodies to fragments and hence, variants of HS3C proteins at, for example, page 9, lines 3-4.

Further, Applicants submit that the invention contemplates a number of specific uses for antibodies which bind amino acid sequences that are variants or fragments of SEQ ID NO: 1. For example, the skilled artisan could use different antibodies to purify proteins having an 1) amino acid sequence that is a variant sequence of SEQ ID NO: 1 verses 2) a HS3C protein sequence having the exact sequence of SEQ ID NO: 1 (See Example XII., page 55, lines 18-23). In another use, antibodies to variants or fragments of the amino acid sequence of SEQ ID NO: 1 can be used for drug screening purposes (see page 46 lines 3-15). Note lines 14-15 on page 46 which state that "antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with HS3C." Additionally, antibodies which specifically bind to variants or fragments of SEQ ID NO: 1 can be used for example in 2D-Page analysis for expression profiling related to toxicology testing,

drug discovery and disease diagnosis. Thus based on the multiple uses contemplated in the Specification, Applicants submit that the skilled artisan would readily know how to use antibodies to a variant or fragment of the sequence of SEQ ID NO: 1.

While Applicants respectfully traverse the above rejection, in order to expedite prosecution of the Application, and solely for purposes thereof, Applicants have rewritten claim 8 in independent form and have included the functional language of "having HS3C activity" to define the recited polypeptide variants. Applicants expressly do not disclaim equivalents which could include antibodies that specifically bind polypeptide variants of SEQ ID NO:1 having biological activities other than HS3C activity. In addition, the fragment language has been deleted from the claims, rendering these issues moot. Applicants believe the claims are allowable in their present form and, therefore, requested withdrawal of this rejection..

**Written Description Rejection under 35 U.S.C. § 112, first paragraph**

Claims 8, 45-46, 48 and 50-57 are rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully traverse this rejection. The Specification provides written description of antibodies to variants to the amino sequence of SEQ ID NO:1 including variants having 90% sequence identity to SEQ ID NO:1 as well as to fragments of SEQ ID NO:1 having biological or immunogenic activity (see page 3, lines 12-20, page 8, lines 16-22 and page 14, line 23 to page 15, line 1). This is further evidenced by the fact that the specification describes the production of antibodies to fragments and hence, variants of HS3C proteins at, for example, page 9, lines 3-9.

However in order to expedite prosecute of the Application, and solely for purposes thereof, Applicants have rewritten claim 8 in independent form and have included the functional language of "having HS3C activity" to define the recited polypeptide variants. Applicants expressly do not disclaim equivalents which could include antibodies that specifically bind polypeptide variants of SEQ ID NO:1 having biological activities other than HS3C activity. In addition, the fragment language has been

deleted from the claims, rendering these issues moot. Applicants believe the claims are allowable in their present form and, therefore, withdrawal of this rejection is believed to be in order.

**Prior Art Rejections under 35 U.S.C. § 103(a)**

All of the prior art rejections under 35 U.S.C. § 103(a) are based upon the combination of Chan et al. (EMBO J 15(5): 1045-54, 1996) with other references including: 1) Harlow et al. (in Antibodies a Laboratory Manual, 1988, Cold Spring Harbor Laboratory Publication, Cold Spring Harbor, NY); 2) U.S. Pat. No. 4,946,778; and 3) U.S. Pat. No. 6,180,370B. In particular, claims 8, 45, 46, 48 and 50-52 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Chan et al. in view of Harlow et al.; claim 45 stands rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Chan et al. in view of U.S. Pat. No. 4,946,778; and claims 45, 56 and 57 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Chan et al. in view of U.S. Pat. No. 6,180,370B. These rejections therefore are respectfully traversed.

As set forth in *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991):

> Rejection of claimed subject matter as obvious under 35 U.S.C. 103 in view of combination of prior art references requires consideration of whether prior art would have suggested to those of ordinary skill in art that they should make claimed composition or device, or carry out claimed process, and whether prior art would also have revealed that such person would have reasonable expectation of success; ***both suggestion and reasonable expectation of success must be founded in prior art, not in applicant's disclosure***. [Emphasis added]

Contrary to the standard set forth by *In re Vaeck*, the Examiner has not shown that the claimed subject matter was suggested by the prior art.

The Office Action states:

> The claimed invention as recited in claim 8 differs from the reference only by the recitation that an isolated antibody which specifically binds to a biologically active fragment or an immunogenic fragment of a polypeptide having an amino acid sequence of SEQ ID NO:1 ***or to a biologically active fragment or an immunogenic fragment of a polypeptide comprising an amino acid sequence at least 90%***

***identical to an amino acid sequence of SEQ ID NO:1***. (Office Action at page 9.) [Emphasis added]

As amended, claim 8 recites:

8. (Once amended.) An isolated antibody selected from the group consisting of:

a) an antibody which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, wherein the antibody binds to an epitope of a polypeptide of SEQ ID NO:1 or SEQ ID NO:3, and

b) an antibody which specifically binds to a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, wherein the antibody binds to an epitope of a polypeptide having a naturally occurring amino acid sequence at least 90% identical to SEQ ID NO:1 or SEQ ID NO:3, said naturally occurring amino acid sequence having HS3C activity.

Thus, the Patent Office position appears to be based on the theory that the applied art is pertinent to antibodies which bind certain polypeptide fragments related to SEQ ID NO:1. While not conceding the propriety of the Patent Office position, claim 8 has been revised to delete recitation of antibodies which specifically bind to fragments of SEQ ID NO:1. In addition, the "variant" language has been revised to recite "an antibody which specifically binds to a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, wherein the antibody binds to an epitope of a polypeptide having a naturally occurring amino acid sequence at least 90% identical to SEQ ID NO:1 or SEQ ID NO:3, said naturally occurring amino acid sequence having HS3C activity." None of the applied art suggests the claimed subject matter. In particular, there is no disclosure of a polypeptide having SEQ ID NO:1, or of any polypeptide at least 90% identical to SEQ ID NO:1. Hence, the cited art could not have guided one to antibodies which specifically bind the recited polypeptides.

These amendments are made solely to expedite prosecution of the subject application. Applicants expressly do not disclaim equivalents which could include antibodies that specifically bind polypeptide variants of SEQ ID NO:1 having biological activities other than HS3C activity.

For at least the above reasons, withdrawal of the § 103 rejections is requested.

## CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650) 855-0555.

Please charge Deposit Account No. 09-0108 in the amount of $400.00 as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. 09-0108.

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: 04 November 2002

Richard C. Ekstrom
Reg. No. 37,027
Direct Dial Telephone: (650) 843-7352

Date: 04 November 2002

Michelle M. Stempien
Reg. No. 41,327
Direct Dial Telephone (650) 843-7219

3160 Porter Drive
Palo Alto, California 94304
Phone: (650) 855-0555
Fax: (650) 849-8886

## VERSION WITH MARKINGS TO SHOW CHANGES MADE

## IN THE SPECIFICATION:

The paragraph beginning at page 1, line 2 has been amended as follows:

This application is a divisional application of U.S. application serial number 09/294,545, filed April 19, 1999, now U.S. Patent No. 6,326,158, issued December 4, 2001, which is a divisional application of U.S. application serial number 08,970,133, filed November 13, 1997, now U.S. Patent No. 5,916,753, issued June 29, 1999, both entitled SH3-CONTAINING PROTEINS, all of which applications and patents are hereby incorporated herein by reference.

## IN THE CLAIMS:

**Claims 1-5, 7, 9-15, 17, 20 and 23-26 have been cancelled.**

**Claim 8 has been amended as follows:**

8. (Once amended.) An isolated antibody [which specifically binds to a polypeptide of claim 1.] selected from the group consisting of:

a) an antibody which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, wherein the antibody binds to an epitope of a polypeptide of SEQ ID NO:1 or SEQ ID NO:3, and

b) an antibody which specifically binds to a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, wherein the antibody binds to an epitope of a polypeptide having a naturally occurring amino acid sequence at least 90% identical to SEQ ID NO:1 or SEQ ID NO:3, said naturally occurring amino acid sequence having HS3C activity.